

## REMARKS

Claims 71-86, 88-91, 93 and 94 are pending and active. Applicants herewith cancel claim 94 and amend claim 71. No new matter is added with this amendment.

The amendment to claim 71 reflects the subject matter in canceled claim 94, and is supported in the specification at page 4, lines 15-23 of the English translation of WO 97/34140.

### **I. Drawings**

The Examiner has requested applicants to submit corrected drawings. Applicants submit a marked up copy of such drawings and will soon supplement this response with the Formal drawings for the draftsman's approval.

### **II. Specification**

Applicants acknowledge the Examiner's statement that the cited documents are not incorporated by reference.

### **III. Rejections under 35 USC § 103**

In paragraph 6, Examiner Sisson rejects claims 71-86, 88-91, 93 and 94 under 35 USC § 103(a) over Williams, US Patent No. 6,020,110, in view of Hollis, WO 93/22678A212.

According to the Examiner, Williams discloses the manufacturing and use of electrodes for the detection of nucleic acids, proteins and antibodies. The "initial gap" of the electrode is alleged to be from 10 to 75  $\mu\text{m}$  and the electrodes can be treated by bonding or absorption of enzymes as well as specific binding partners, for example DNA, avidin, biotin and so on. The Examiner concedes that Williams does

not teach that the gap narrows to where it ranges from 1  $\mu\text{m}$  to that of a large molecular complex.

In paragraph 8, the Examiner states that Williams teaches that the apertures may be of virtually any shape, including circles, squares, rectangles or bands. In paragraph 9, the Examiner states that Williams teaches separating working and reference electrodes via a polyester substrate, which is construed as serving as an insulating material. In paragraph 10, the Examiner states that Williams teaches that the working and counter electrodes comprise silver and gold or carbon and that a reference electrode can comprise silver. In paragraph 11, the Examiner states that: "The aspect that the electrodes are printed on a flat polyester substrate (column 4) meets the I[sic]mitation that the electrodes constitute 'A layer on a plane insulating support material.' "

In paragraph 12, the Examiner cites Hollis for teaching that the gap in the insulating material is 2  $\mu\text{m}$  wide but the spacing between the upper and lower electrodes is of the order of length of the target DNA molecule. In paragraph 13, the Examiner cites Hollis at page 25 for teaching that various materials can be incorporated into the substrate. The Examiner alleges in paragraph 14 that Figure 1 shows a device where the electrodes are arranged in a substantially planar manner as well as being stacked. The electrode leads are alleged to be surrounded by a non-conductive substrate so are insulated from one another.

In paragraph 15, Examiner Sisson concludes that in view of the teachings in the prior art and the motivation for arranging electrodes such that the gap between the electrodes approximates the size of a large molecular complex, it would have been obvious to one of ordinary skill in

the art at the time of the invention to have incorporated the sensor and methodologies of Hollis into the disclosure of Williams for purposes of achieving greater sensitivity.

Applicants respectfully traverse this rejection. In further response, applicants have amended claim 71 to recite that each of said electrode structures is incorporated in a planar insulating support material for planarization. In the Office Action at paragraph 22, the Examiner found Applicants' previous arguments unpersuasive because claim 71 was not limited to an electrode arrangement that was substantially planar. In order to clarify the present invention, Applicants have amended claim 71 to recite this feature. The support for this amendment can be found in the specification at page 4, lines 15-23, as indicated above.

In yet further response to comments in paragraphs 19 and 20, applicants assert that Examiner Sisson has only selectively read Williams. Specifically, the Williams' structure, which may have been "printed" onto a planar surface is, in fact, then **covered**, except in the area of the apertures (see Figure 4, referential 3 and paragraph 2, lines 10 to 53). Consequently, no space is defined between the electrodes and this limitation of claim 71 is not met by Williams. In contrast to the claimed invention, Williams teaches a wall-like structure between the electrodes. Thus, when read as a whole, Williams does not suggest the present invention.

Applicants reiterate their previous comments about Hollis. That is, figure 1 of Hollis *et al.* depicts a device where the electrodes are arranged in an interdigital manner of two electrode structures. However, such structures are neither arranged in a substantially planar manner, nor

are they stacked. In contrast, the surface of the first electrode structure is about 4.500 Å below the surface of the second electrode structure (their thickness is almost identical, and the first structure is deposited in the well sites prepared by etching out about 4.000 Å SiO<sub>2</sub> plus 500 Å of the mask material). Indeed, an arrangement in a substantially planar manner **must necessarily be avoided** in order to avoid **shorting of the electrodes**.

This is achieved in that the electrode thickness is about 2.300 Å (300 Å of Ti and 2.000 Å of Au) so that about 2.400 Å distance remains between the upper surface of the lower electrode structure and the lower edge of the upper electrode structure. Thus, the spacing between the upper and lower electrodes which, according to Hollis, “is of the order of the length (or diameter in solution) of the target DNA molecule” (and which is 2.200 Å, according to the description of the preparation in connection with figure 5) is a **vertical spacing**.

Applicants incorporate previous arguments (see Response filed January 9, 2003, page 12, last paragraph bridging lines 1 to 3 of page 13) with regard to Hollis. Applicants again assert that when Williams and Hollis are carefully read, in their entirety and not selectively, neither reference, alone or in combination, suggests or guides the skilled artisan toward the claimed invention. In view of these arguments and the above amendment, applicants respectfully request the Examiner to reconsider the rejection under 35 USC § 103.

## CONCLUSION

Applicants respectfully request Examiner Sisson to consider the above remarks and enter the above amendment thereto. Applicants further assert that entry of the amendment is proper as it places this case in condition for allowance. Early notification of allowance is earnestly requested. Examiner Sisson is encouraged to contact the undersigned attorney for applicants at 202-912-2142 for any reason related to the advancement of this case.

Respectfully submitted,

Date: July 21, 2005

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